



Armed Forces College Of medicine AFCM

**May your morning be as sweet as
the sugar!
As wonderful as the sound of music,
And as beautiful as you truly are,
So have a lovely day,
Wish you a very good morning for today!**



Pathology of rheumatic fever

Prof. Eman Abdelbary

Intended Learning Objectives (ILOs)



By the end of this lecture the student will be able to:

1. Identify the aetiology, diagnostic criteria and complications of rheumatic fever
2. Summarize the pathogenesis and features of rheumatic fever
3. Correlate between pathological features, laboratory findings and clinical course of rheumatic lesions.

Lecture plan



1. Part 1 (10 min): definition, etiology & pathogenesis of rheumatic fever
2. Part 2 (20 min): pathology of cardiac & extracardiac lesions
3. Part 3 (10 min): diagnosis of rheumatic fever

Rheumatic fever



Definition:

An immunologically mediated, multisystem inflammatory disease that occurs after group A β -hemolytic streptococcal infections

***Rheumatic heart disease* is the cardiac manifestation**

Predisposing factors:

- 1. Young age: 5-15 years**
- 2. Overcrowding, bad ventilation (low socioeconomic conditions)**
- 3. Familial predisposition**
- 4. Genetic susceptibility**



Rheumatic fever



pathogenesis:

Streptococcal throat infection

Release of M protein (from bacterial cell wall)

Has antigenic similarity to cardiolipin

Formation of Ab & CD4+ T cells against M protein
e.g. ASO

Ab & T cells cross-reacts with cardiac tissue

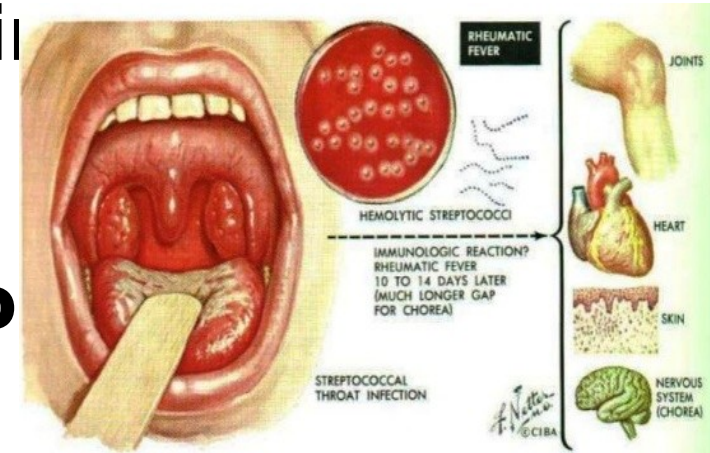
Inflammatory response & Tissue damage

Rheumatic fever



Pathogenesis: Antigenic similarity (cross-reactivity)

- It is a hypersensitivity reaction caused by antibodies against group A Beta hemolytic streptococci
- **It** occurs 2- 3 weeks after upper respiratory tract infection (time needed to generate the immune response)
- The bacteria is **absent** from the blood or other sites of rheumatic lesions.



Rheumatic fever



Pathogenesis: Antigenic similarity (cross-reactivity)

Antibodies & CD4+ T lymphocytes against streptococcal antigens (M protein) cross-react with human tissue antigens (mainly CT glycoproteins & sarcolemma of muscles) activate complement, macrophages & initiate cytokine-mediated inflammatory response Tissue damage



Etiology and pathogenesis (Quiz)

Q: List two predisposing factors of rheumatic fever?

Answer:

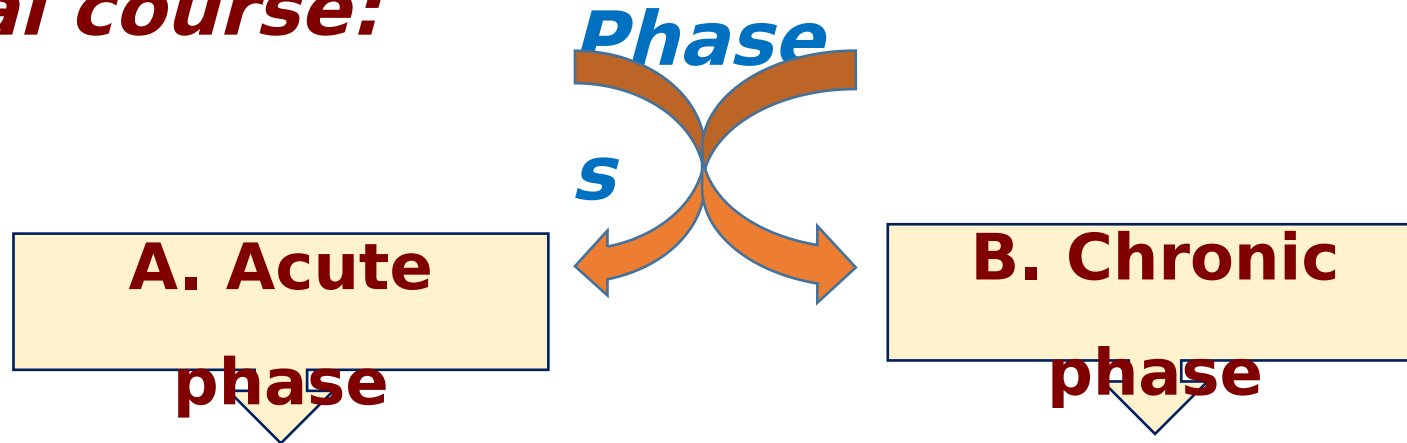
Predisposing factors are:

- 1. Young age: 5 - 15 years**
- 2. Overcrowding, bad ventilation (low socioeconomic conditions)**
- 3. Familial predisposition**

Rheumatic fever



Clinical course:



Heart & extracardiac tissues (joints, brain, skin, etc.)

Heart only, specially cardiac valves.

N.B.: Extra-cardiac lesions **resolve completely** without chronicity.

➤ **Clinical manifestations of the chronic phase usually appear**

Rheumatic fever



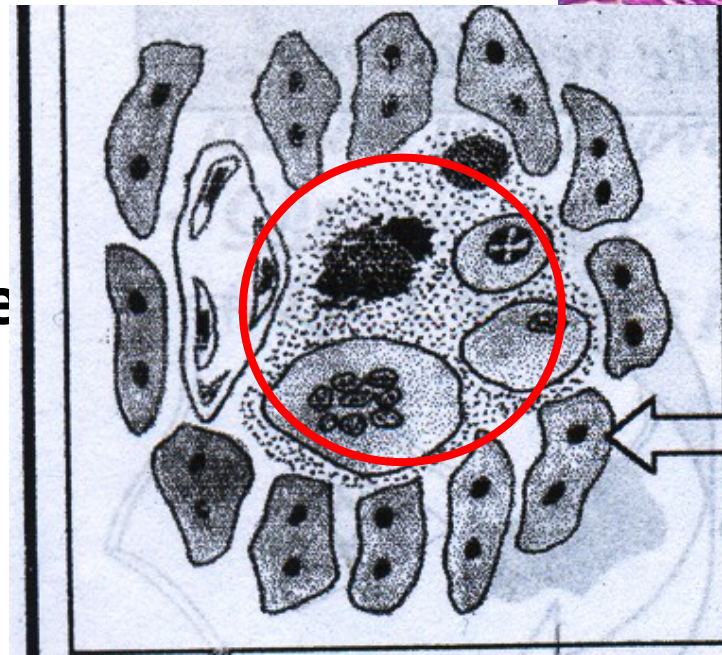
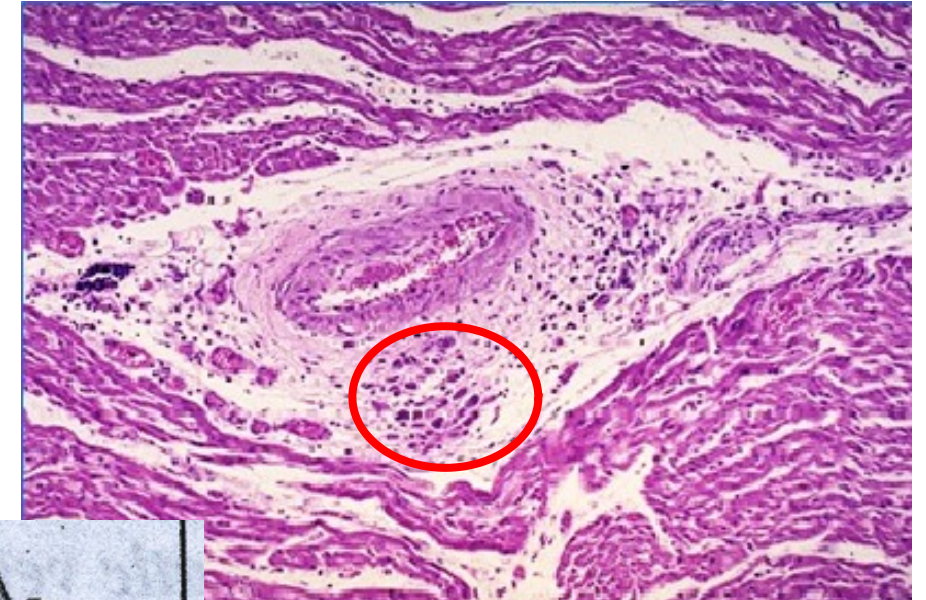
Pathological reaction:

Aschoff bodies:

Pathognomonic for rheumatic fever

Grossly:

- **Paravascular,**
- **Small sized (1-2 mm),**
- **Hardly seen by naked eye**
- **Gray white nodules**



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Rheumatic fever



Pathological reaction: Cont. Aschoff

bodies:

Microscopically:

- Central area of **fibrinoid necrosis** (fragmented collagen), surrounded by **plasma** cells & activated mononuclear or multinucleated macrophages (**i.e. Anitschkow cells**)
- Later: the nodule is surrounded by fibrosis (develops after years)



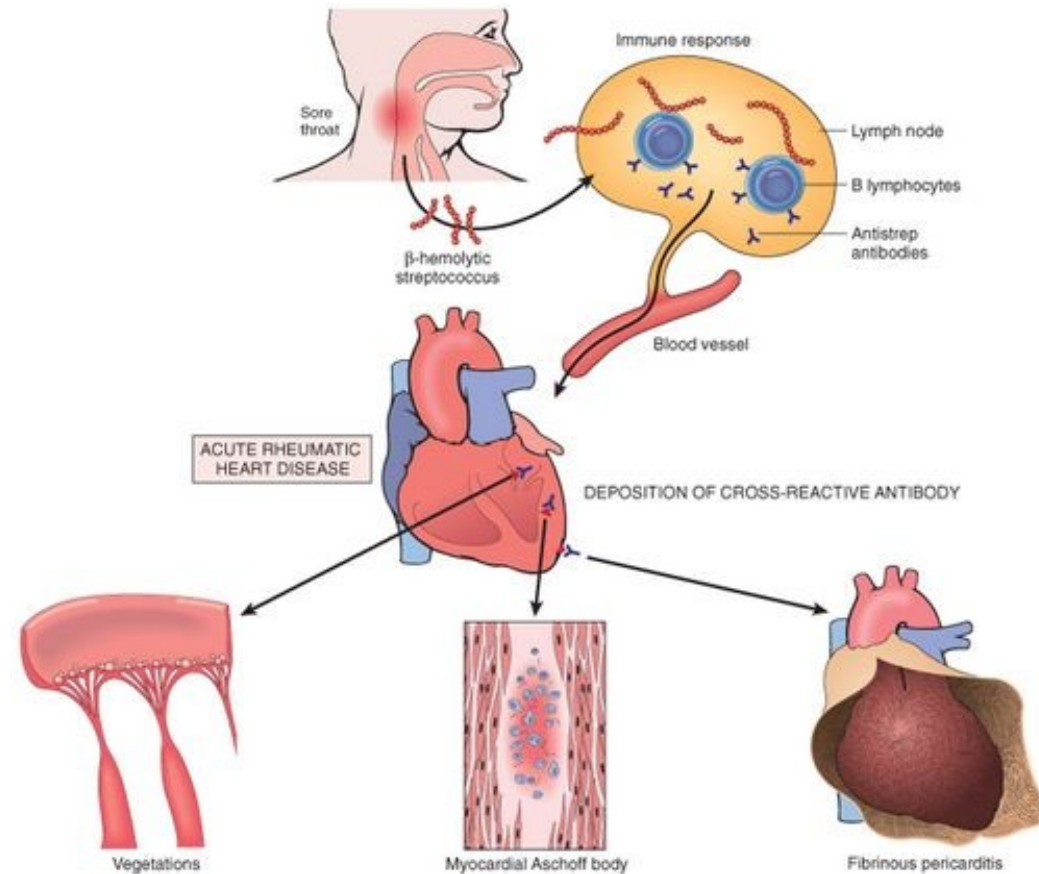
Rheumatic fever



Pathological reaction: Cont.

I. Rheumatic heart disease:

**All layers are affected
(Pancarditis)**



<http://www.stepwards.com/wp-content/uploads/2016/01/Rheumatic-Heart-Disease-Pathogenesis.jpg>

Rheumatic fever



Pathological reaction: Cont.

I.A. Rheumatic myocarditis:

❑ ***Acute phase:***

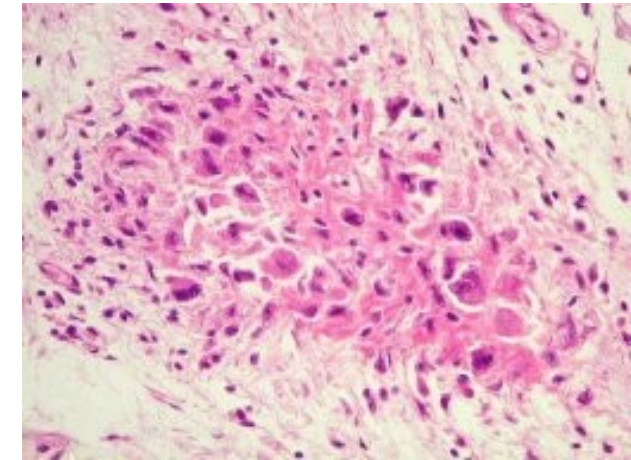
❖ **Edema & Aschoff bodies in the interstitium of the myocardium**

❖ **Rarely severe → fulminant myocarditis**
Acute heart failure & death.

❑ ***Chronic phase:* Myocardial fibrosis**



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Rheumatic fever



Pathological reaction: Cont.

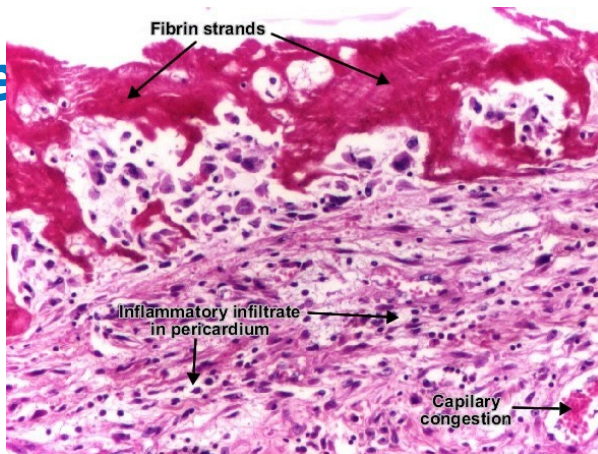
I.B. Rheumatic pericarditis:

Acute phase: serofibrinous pericarditis

Fibrin threads are deposited between visceral & parietal layers



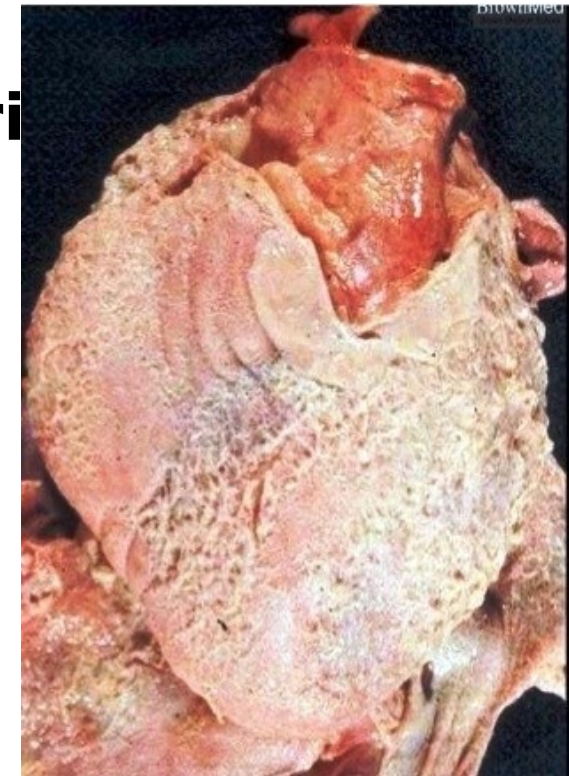
Bread and butter appearance (friction rub)



http://2.bp.blogspot.com/-f14SQoQznGU/T446UdFH4JI/AAAAAAAAAHcc/SzR8i96r_IQ/s1600/fibrinous_pericarditis_detail.jpg



(Cardio-Pulmonary Module)



http://www.brown.edu/Courses/Digital_Path/systemic_path/cardio/CV85.jpg

Rheumatic fever

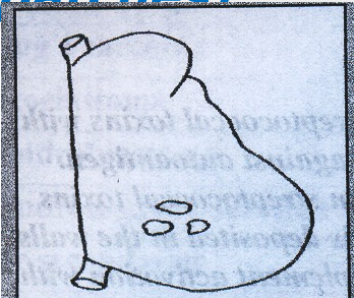


Pathological reaction: Cont.

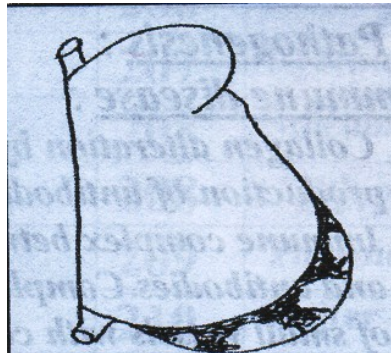
I.B. Rheumatic pericarditis: either resolves or becomes

Chronic phase: Fibrosis
chronic results in

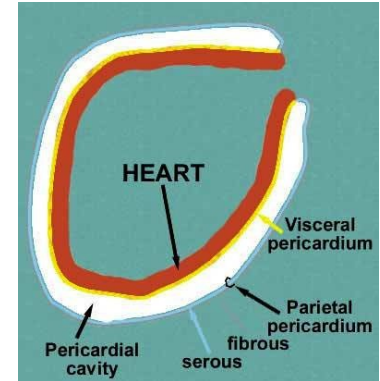
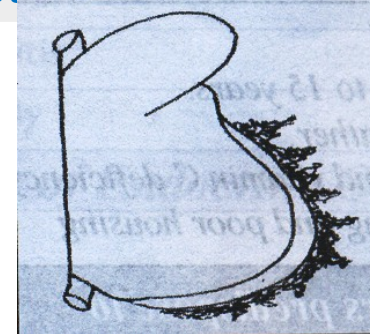
White patches of fibrosis on the heart surface (*milk patches*)



Adhesions between both layers of pericardium



Adhesions of pericardium & mediastinum (*adherent mediastino-pericarditis*)



Rheumatic fever



Pathological reaction: Cont.

I.C. Rheumatic endocarditis:

Lt. side is more commonly affected.

I.C.i: Mural endocarditis:

➤ ***Acute phase:*** Aschoff bodies in the mural endocardium lining of the **posterior wall of Lt. atrium**

➤ ***Chronic phase:*** white fibrous patch of posterior wall of Lt. atrium (***MacCallum's***



https://upload.wikimedia.org/wikipedia/commons/thumb/9/97/Rheumatic_heart_disease%2C_gross_pathology_20G0013_lores.jpg/220px-Rheumatic_heart_disease%2C_gross_pathology_20G0013_lores.jpg

New Five Years Program
patch) due to healing of Aschoff bodies

(Cardio-Pulmonary Module)

Rheumatic fever



Pathological reaction: I.C. Rheumatic endocarditis: cont.

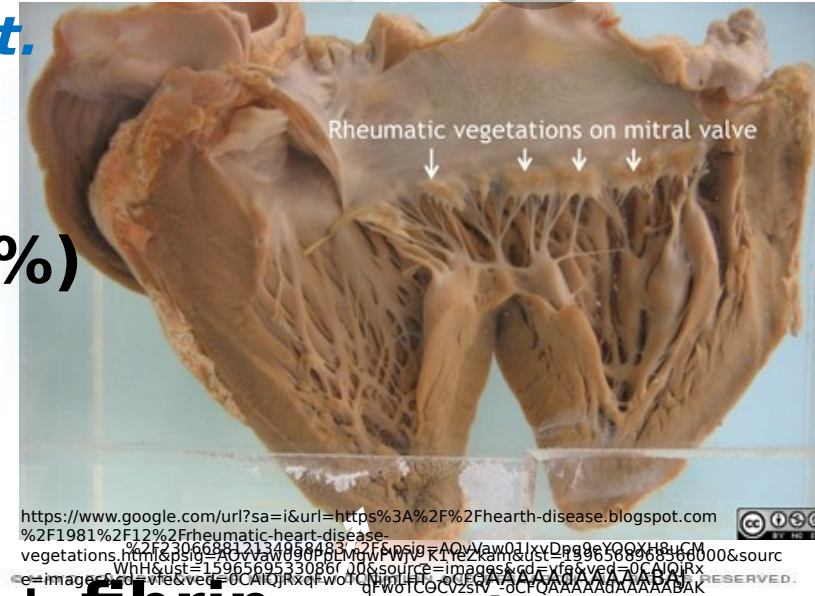
I.C.ii: Valvular endocarditis: (most important)

(Mitral alone 75%, mitral & aortic 25%)

➤ **Acute rheumatic valvulitis:**

- **Cusps:** swollen (inflammation, edema)
- **Vegetations (thrombi):** formed of platelets + fibrin

Site: - Along the **line of cusp closure** (due to endothelial damage) i.e. atrial surface of mitral & tricuspid valves, ventricular surface of aortic & pulmonary valves.



- **Multiple, small, gray lesions, firmly adherent to the**

Rheumatic fever



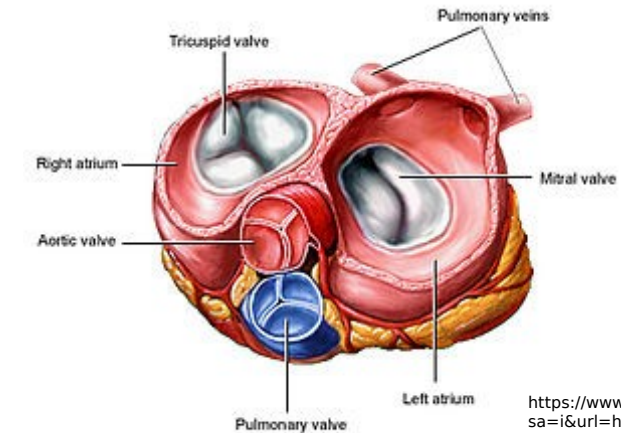
Pathological reaction: Cont.

I.C. Rheumatic endocarditis:

I.C.ii: Valvular endocarditis:

➤ **Chronic rheumatic valvulitis:**

Organization & fibrosis → **the cusps appear fibrotic, thick,**
irregular with calcified patches → **stenosis (*fish mouth,***
***button hole*). incompetence or double valve**

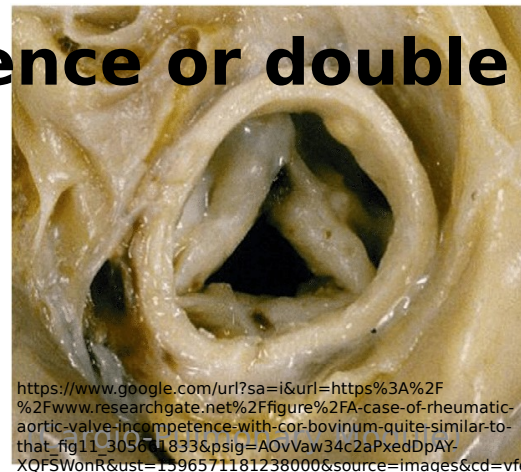


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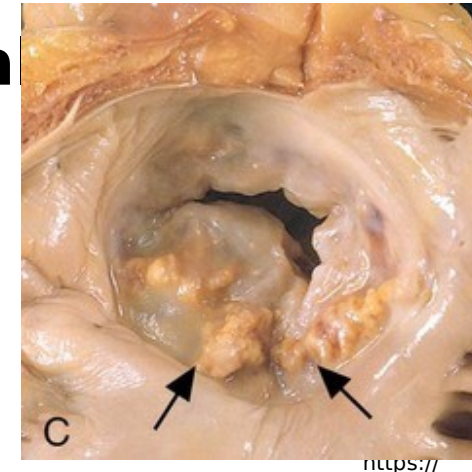


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https://www.google.com/url?sa=i&url=https%3A%2F%2Fwww.researchgate.net%2Ffigure%2Ffigure%2FA-case-of-rheumatic-aortic-valve-incompetence-with-cor-bovinum-quite-similar-to-that_fig11_303611833&psig=AOvVaw34c2aPxdDpAY-XQFSWohR&ust=1596571181238000&source=images&cd=vfe&ved=0CAIQjRxqFwoTCMi_j9fb_-oCFQAAAAAAdAAAAABAS



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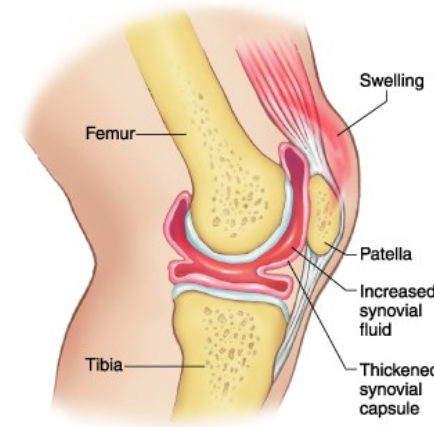
Rheumatic fever



Pathological reaction: Cont.

II.1. Rheumatic Arthritis

- **Migratory (fleeting) arthritis**
- **Affects large joints**
- **Heals with no deformity** (articular cartilage is not affected)
- **Grossly:** the synovium is thick, red & granular
- **Microscopically:** Acute serofibrinous synovitis (congestion, edema, inflammatory cells)



<https://image.slidesharecdn.com/acute-rheumatic-fever-170419014244/95/acute-rheumatic-fever-170419014244.jpg?cb=1493430181>

Rheumatic fever



Pathological reaction: Cont.

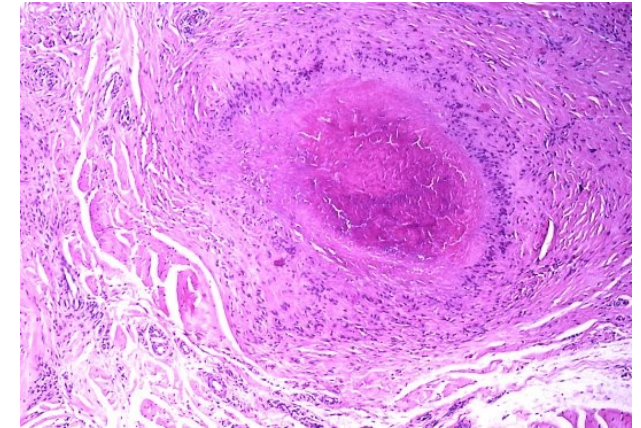
II.2. Rheumatic skin lesions:

A) subcutaneous nodules

- ❑ Small, firm nodules
- ❑ 2-20 mm in diameter,
- ❑ Over bony prominences & extensor surface of limbs
- ❑ Microscopically *similar to Aschoff bodies*



<https://escholarship.org/content/qt4zx6v9j3/inner/1.jpg>



http://grahm.himelstead.com/rheumatoid_nod_s89-2617-1.jpg

B) Erythema marginatum:

Macules with erythematous edge & central clear



Rheumatic fever



Pathological reaction: Cont.

II.3. Rheumatic brain lesion: (Rheumatic chorea)

- ❑ A ***reversible*** neurological disorder characterized by rapid involuntary purposless movements
- ❑ Due to inflammation of the basal ganglia

II.4. Rheumatic lung lesions: Very rare e. g. Fibrinous pleurisy or rheumatic pneumonitis

II.5. Rheumatic arteritis: Type III hypersensitivity reaction.



Which valves are commonly affected by rheumatic fever:

- A. Tricuspid , mitral
- B. Mitral , Aortic
- C. Tricuspid , pulmonary
- D. Aortic , pulmonary



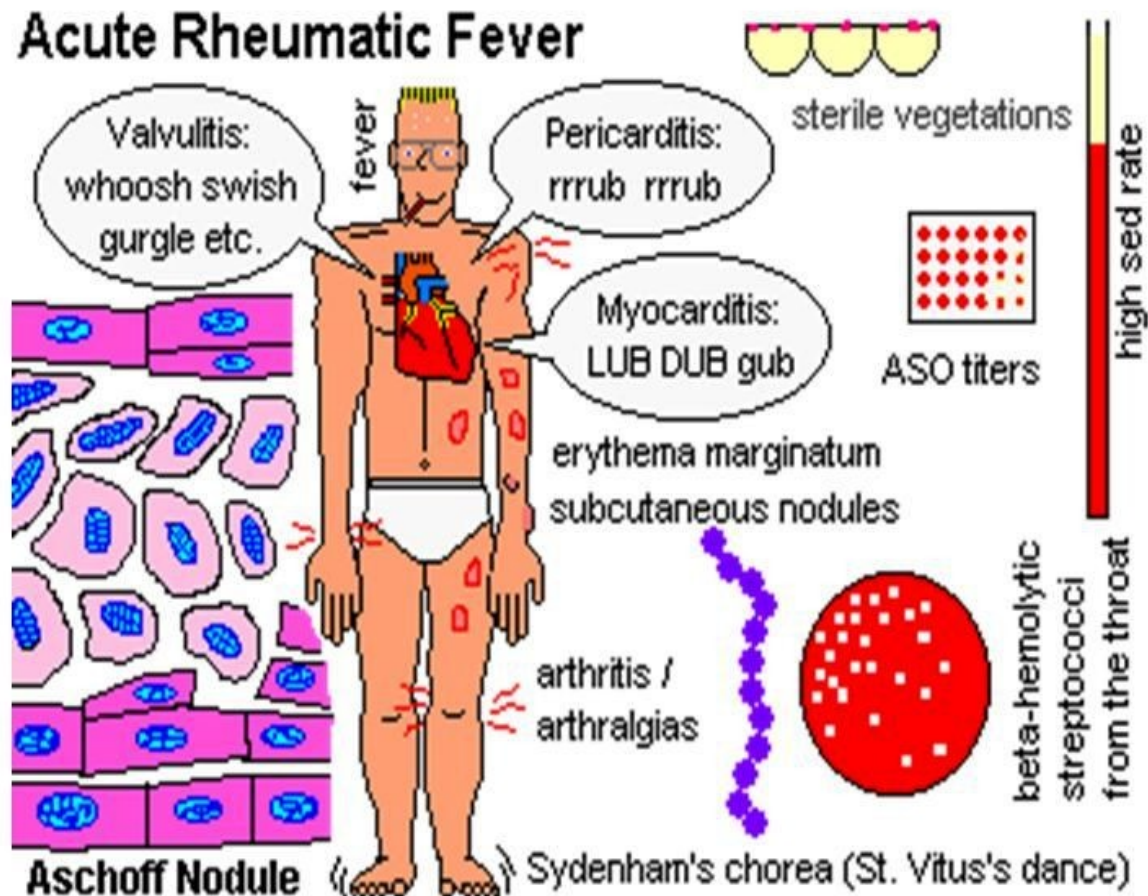
Which valves are commonly affected by rheumatic fever:

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- B. Mitral , Aortic**
- C. Tricuspid , pulmonary
- D. Aortic , pulmonary

Rheumatic fever



Clinical Manifestations



Rheumatic fever



Diagnosis: Modified Jones criteria:

Major criteria:

- Carditis (***most common***)
- Arthritis
- Erythema marginatum
- Subcutaneous nodules
- Rheumatic chorea

Minor criteria:

- Fever
- Arthralgia
- Leucocytosis
- ↑ Erythrocyte sedimentation rate (ESR)
- C-reactive protein (CRP)
- Prolonged PR interval

Rheumatic fever



Diagnosis of rheumatic fever:

2 major criteria + evidence of streptococcal infection

OR

1 major criterion + 2 minor criteria + evidence of streptococcal infection

N.B. Evidence of streptococcal infection:

- Throat culture
- Serology for streptococcal antigen or antibody

e.g. Antistreptolysin O (ASO), Antistreptococcal DNase

Rheumatic fever



Complications:

- 1) Heart failure: Due to: -fulminant myocarditis (in **acute** phase),
-valvular lesions & pericardial adhesions (in **chronic** phase) →
- 2) Increased risk of → infective endocarditis. →
- 3) Valve deformity → leads to hemodynamic abnormalities
more fibrosis
- 4) Tight mitral stenosis atrial fibrillation Lt. atrial



Diagnosis of rheumatic fever (Quiz)

A 12 years old girl presented to her family physician complaining of fever and pain & swelling in the left knee joint that persisted for 3 days then disappeared, and reappeared at the right ankle. Her Laboratory findings showed leucocytosis and elevated ESR. Which of the following statements describes her medical condition?

- A. She has one major & two minor John's criteria.
- B. She has four minor John's criteria
- C. The patient can be diagnosed as acute rheumatic fever
- D. If her ASO titer is elevated, rheumatic fever is the diagnosis



Diagnosis of rheumatic fever (Quiz)

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Key points



- Rheumatic fever is an immunologically mediated, multisystem inflammatory disease
- Pathogenesis of rheumatic fever involves antigenic similarity theory
- Cardiac lesions may be acute or chronic, while all extra cardiac lesions resolve completely without chronicity
- Aschoff body is pathognomonic for rheumatic fever
- Rheumatic heart disease leads to pancarditis
- Rheumatic arthritis is a fleeting arthritis affecting large joints
- Modified Jhon's criteria are used for diagnosis of rheumatic fever

Suggested Textbooks



1. Mitchell R. Blood vessels. In Robbins and Cotran pathologic basis of disease, 9th edition. Kumar, Abbas & Aster (eds). Elsevier Saunders. Pages 487 to 491.
2. Cardiac pathology. In USMLE step 1 lecture notes, 2017. Kaplan INC, New York. Pages 112 -125



Thank you